

June 18, 2001

Cynthia Graham, Ph.D.  
Bayer Corporation  
100 Bayer Road  
Pittsburgh, PA 15205-9741

Dear Dr. Graham:

Thank you for Bayer's submission of Cyclohexyl isocyanate (CHI, CAS No. 3173-53-3) to the RTK HPV Challenge Program. EPA has conducted a preliminary review of the submission and will proceed to post it on the program's Web site. However, we note that the test plan for Cyclohexyl isocyanate proposes reduced testing on the basis that it is a closed-system intermediate.

As you know, EPA has highlighted animal welfare considerations in its approach to the Challenge Program. As described in a recent Federal Register notice entitled "Data Collection and Development of HPV Chemicals" (65 FR 81686), EPA has asked that sponsors observe a number of principles included in a letter to sponsor companies dated October 14, 1999 (<http://www.epa.gov/chemrtk/ceoltr2.htm>) (enclosure). It is the intention of the Agency that the HPV Challenge program should proceed in a manner consistent with this guidance.

The above guidance is relevant to your proposals because participants are asked to defer animal testing on individual chemicals (i.e., those not part of a category) until November, 2001, or until 2003 if a test substance is a closed-system intermediate.

Bayer indicates in its test plan that CHI meets the closed-system intermediate criteria for reduced testing under the HPV Challenge program. However, the Test Plan for CHI does not provide adequate documentation to substantiate such a claim. For example, to be eligible for this provision it is necessary to establish that all sites in the United States manufacture and handle the chemical in a manner consistent with the definition of closed-system intermediate. In addition, your submission states that CHI is stored onsite and transported to other sites, a situation which, depending on the number of sites involved, may warrant full testing even though the chemical upon further analysis may be judged a closed-system intermediate. Bayer needs to carefully evaluate whether CHI satisfies the criteria for a closed-system intermediate in accordance with EPA's "Guidance for Testing Closed System Intermediates for the HPV Challenge Program" (<http://www.epa.gov/opptintr/chemrtk/closed9.htm>). Please consult the guidance document cited above for more details.

EPA requests that Bayer consider these concerns and advise the Agency within 30 days of any modifications to its submission.

The HPV Challenge is a voluntary program whose successful implementation will depend upon the good faith effort and cooperation of all parties. We appreciate the spirit of cooperation and commitment that has characterized this initiative to date.

Thank you again for your commitment to participate in the HPV Challenge program. If you wish further clarification, please contact Rich Hefter at 202-260-3470 or visit the Web site at [www.epa.gov/chemrtk](http://www.epa.gov/chemrtk).

Sincerely,

/s/

Oscar Hernandez, Director  
Risk Assessment Division

cc: W. Sanders  
C. Auer

Enclosure